

2 WHAT IS CLAIMED IS:

- 3 1. A method of inhibiting expression of a target allele in a cell comprising at least two
4 different alleles of a gene, the method comprising administering to the cell an siRNA
5 specific for the target allele.
- 6 2. The method of claim 1, wherein the target allele is correlated with a disorder
7 associated with a dominant gain of function mutation.
- 8 3. The method of claim 2, wherein the disorder is selected from the group of
9 amyotrophic lateral sclerosis, Huntington's disease, Alzheimer's disease, and
10 Parkinson's disease.
- 11 4. A method of treating a subject having a disorder correlated with the presence of a
12 dominant gain of function mutant allele, the method comprising administering to the
13 subject a therapeutically effective amount of an siRNA specific for the mutant allele.
- 14 5. The method of claim 4, wherein the siRNA is targeted to the gain of function
15 mutation.
- 16 6. The method of claim 4, wherein the disorder is selected from the group of
17 amyotrophic lateral sclerosis, Huntington's disease, Alzheimer's disease, and
18 Parkinson's disease.
- 19 7. The method of claim 4 wherein the disease is amyotrophic lateral sclerosis.
- 20 8. The method of claim 7 wherein the allele is SOD1.
- 21 9. The method of claim 8, wherein the mutant allele comprises a point mutation.
- 22 10. The method of claim 8, wherein the point mutation is a guanine: cytosine mutation.
- 23 11. The method of claim 8, wherein the mutation is G256C.
- 24 12. The method of claim 8, wherein the mutation is G281C.
- 25 13. The method of claim 8 wherein the siRNA comprises a sequence as set forth in Figure
26 1A.
- 27 14. An siRNA comprising a sequence as set forth in Figure 1A.
- 28 15. A p10 mutant siRNA comprising the sequence as set forth in Figure 1A.
- 29 16. A p9 mutant siRNA comprising the sequence as set forth in Figure 1A.
- 30 17. A G93A SOD1 shRNA comprising the sequence as set forth in Figure 3A.
- 31 18. An expression construct comprising the shRNA of claim 13.
- 32 19. A therapeutic composition comprising the siRNA of claim 10-12, and a
33 pharmaceutically acceptable carrier.

- 34 20. A therapeutic composition comprising the shRNA of claim 13, and a pharmaceutically
35 acceptable carrier.